REMARKS

Corrections to SEQUENCE LISTING

SEQ ID NO: 76

The sequence for SEQ ID NO: 76 was given incorrectly in the SEQUENCE LISTING as ATACA GGGGAT. This incorrect sequence is an obvious typographical error; as seen in Table 1 on page 49 of the description, the correct sequence for SEQ ID NO: 76 (the 5′ splice donor for Exon 10) is CACAG GTATTA. The sequence ATACA GGGGAT is actually the correct sequence for SEQ ID NO: 77 (the 3′ splice acceptor for Intron 1), as shown in Table 1 and SEQ ID NO: 77 in the SEQUENCE LISTING. We are herewith providing a substitute paper copy of the SEQUENCE LISTING and substitute computer readable copy (CRF), and request that the SEQ ID NO: 76 in the SEQUENCE LISTING be amended to read CACAG GTATTA to be consistent with the description. The SEQUENCE LISTING information recorded in computer readable form is identical to the written paper copy.

Status of the Claims:

Claim 58 has been cancelled without prejudice. Claims 48-57 and Claims 59-69 are pending in the application.

Rejection under 35 U.S.C. §112, 1st Paragraph

Claim 58 stands rejected under 35 U.S.C. § 112, first paragraph "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." [Office Action, page 2.]

As Applicants have canceled Claim 58, Applicants respectfully point out that the rejection is now moot. However, Applicants wish to point out that the rejected claim, which claim was substantially copied from claim 4 of the McKiernan et al. '098 patent (U.S. Patent No. 6,087,098) to provoke an interference, has been canceled as claims 1-6 of the McKiernan et al. '098 patent were not enabled, for the reasons that Applicants have presented in their response sent on June 2, 2003.

Claim 58 was directed to specific primers for use in an RT-PCR process to detect an increase in MN gene expression. The Office Action states on page 2, that "applicant has disclosed that an increase in MN protein is diagnostic of neoplastic and/or preneoplastic diseases and gives numerous examples including renal carcinoma. In addition there is basis for the patenting of a generic RT-PCR process to detect an increase in MN gene expression, however, there is not explicit

elaboration of the claimed RT-PCR process (i.e., the primers) to detect an increase in MN gene expression" [Emphasis added].

Written Description Requirement for Claim 58

Although the rejection of claim 58 is now moot in view of the cancellation of that claim, Applicants respectfully point out in regard to the written description requirement that a "specification is directed to those skilled in the art and need not teach or point out in detail that which is well-known in the art." [In re re Myers, 161 USPQ 668, 671 USPQ 668, 671 (CCPA 1969)]. Moreover, "A patent need not teach, and preferably omits, what is well known in the art." [Spectra-Physics, Inc. v. Coherent, Inc., 3 USPQ 2nd 1737, 1743 (Fed. Cir. 1987); emphasis added.] Therefore, Applicants submit that it would be understood by one skilled in the art at the time the application was filed that Applicants had possession of the primers for use in the RT-PCR, as the Examiner admits that the Applicants had possession of a generic RT-PCR process to detect an increase in MN gene expression.

Applicants respectfully offer that at the time the instant application was filed, there was ample direction for one of skill in the art to prepare primers for use in RT-PCR, given the sequence of the MN gene. See, for example, Saiki, R.K., PCR Protocols: A Guide to Methods and Applications (eds. Innis,

M.A. et al.) Academic Press, San Diego, CA (1990): ". . . [G]enomic amplifications are usually quite straightforward and are not necessarily more complicated than those of simpler systems. This equivalence can be attributed to the high specificity of the priming step. . . ." Further, "Some simple rules aid in the design of efficient primers" (page 9, Innes, M.A. and Gelfand, D.H., ibid; emphasis added). Therefore, the specificity for PCR primers directly depends upon the sequence of the gene in question.

Applicants submit that there would be no inventive step in preparing specific RT-PCR primers to detect an increase in MN gene expression, given the sequence for the MN gene. Further, Applicants point out that the two particular primers specified in Claim 4 of the McKiernan et al. '098 were not enabled for RT-PCR, for the reasons given previously in Applicants' Preliminary Amendment (dated July 11, 2001) and reiterated below.

Provisional Double Patenting Rejection

The Office Action at page 3 rejects Claims 48-51 "under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-3 of U.S. Patent No. 6,027,887." Further, the Office Action rejects Claims 52-57 and 59-69 "under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claim 1-13 of U.S. Patent No. 6,027,887 in view of Samid [US Patent No.: 5,605,930 (1997)]." [Office Action, page 3.] That Office Action points out at page 3 that "[a] timely filed terminal disclaimer in compliance with 37CFR 1.32(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application."

Such a terminal disclaimer is enclosed. Applicants respectfully conclude that this rejection is addressed by the terminal disclaimer. The Commissioner is hereby authorized to charge the $110 terminal disclaimer fee to the credit card indicated on the enclosed Credit Card Payment Form.

Response to Applicant's Amendment/Arguments

Utility of McKiernan et al. Patent [US 6,087,098]

The Examiner's states that "[t]he applicant presents numerous paragraphs of arguments including reasoning as to why the McKiernan et al. patent [US 6,087,098 (2000)] lacks utility and is not enabled. In response, the examiner must admit that he agrees with the applicant's reasoning. . . ." (Office Action, page 4).

Applicants thank the Examiner for his remarks regarding the lack of utility and lack of enablement of the

McKiernan et al. '098 patent. As Applicants pointed out in their response dated June 2, 2003, the MN antigen is expressed by most tumor types. Therefore, the RT-PCR detection of MN mRNA extracted from blood can be used to screen for the presence of preneoplastic/ neoplastic disease, but not to diagnose a specific type of preneoplastic/neoplastic disease, the latter being the premise on which McKiernan et al. had based the use of RT-PCR for kidney cancer diagnosis (the '098 patent).

Further, Applicants would like to reiterate comments made previously in their Preliminary Amendment and Request for Declaration of an Interference with U.S. Patent No. 6,087,098, dated July 11, 2001, regarding the enablement of the two primers specified in the McKiernan et al. '098 patent. As Applicants pointed out in that Preliminary Amendment, SEQ ID NO: 2 of the '098 patent would not specifically hybridize under the McKiernan et al. experimental conditions to the MN cDNA and therefore would not be effective in amplifying a 386 base pair (bp) fragment of the MN cDNA. When the SEQ ID NO: 2 primer of the McKiernan et al. '098 patent is compared to the MN cDNA, only a 92.9% similarity in 14 bp overlap with MN cDNA is found. That means that the primer is not correct and would provide no RT-PCR product under the experimental conditions of the McKiernan et al. patent. The calculated annealing temperature of the primer is 48°C using Oligo software or 52°C using the formula T = 4(G +

C) + 2(A + T), whereas the RT-PCR was performed at 57°C. That means the RT-PCR could not work performed with the SEQ ID NO: 2 primer under the McKiernan et al. experimental conditions.

However, one of skill in the art given the MN cDNA sequence that is SEQ ID NO: 1 and shown in Figure 1 of the Zavada et al. U.S. patents and applications would be able to find correct primers to amplify fragments of the MN cDNA for diagnostic/prognostic assay.

Request for Declaration of Interference

The Examiner states on page 4 of the Office Action that

> as regards the declaration of an interference with the claims of the McKiernan et al. patent [U.S. 6,087,098 (2000)], the examiner finds the applicant's arguments unpersuasive. McKiernan et al. is claiming a patentably distinct species which falls within the broader scope of the instant claims and those of US Patent No. 6,027,887.

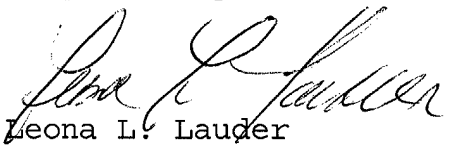
In view of the Examiner's previous remarks that he "must admit that he agrees with the applicant's reasoning" in regard to why the McKiernan et al. '098 patent lacks utility and is not enabled (Office Action, page 4), Applicants respectfully accept the Examiner's decision not to declare an interference. Applicants respectfully point out that the acceptance of the Examiner's decision does not constitute an admission that the

instant application does not satisfy the written description requirement for specific primers for an RT-PCR process, but is based on the particular circumstances concerning the lack of utility of the claims of McKiernan et al. '098 patent.

CONCLUSION

Applicants respectfully conclude that the claims as amended are in condition for allowance, and earnestly request that the claims be promptly allowed. If for any reason the Examiner feels that a telephone conference would expedite the prosecution of the instant application, the Examiner is invited to telephone the undersigned Attorney for the Applicants at 415-981-2034.

Respectfully submitted,



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Dated: December 3, 2003